REMARKS

In response to the Restriction Requirement mailed September 18, 2006, Applicant provisionally elects, with traverse, the claims of Group IA (claims 1-32 and 43-60), directed to a method to enhance recombinant adeno-associated virus (rAAV) transduction of a mammalian cell, which includes contacting a mammalian cell with at least one rAAV and at least two agents in an amount effective to additively enhance rAAV transduction, and a method to enhance rAAV transduction of a mammalian cell, comprising: contacting the mammalian cell with at least one rAAV and at least one agent that alters rAAV endocytosis, rAAV trafficking or processing in intracellular compartments, viral nucleic acid or protein degradation, nuclear transport of virus or viral genome, effective to enhance rAAV transduction, with the proviso that the agent is not an inhibitor of proteosome proteolytic activity.

In response to the election of species from i) a method which includes contacting a mammalian cell with at least one rAAV and at least two agents in an amount effective to additively enhance rAAV transduction or a method which includes contacting the mammalian cell with at least one rAAV and at least one agent that alters rAAV endocytosis, rAAV trafficking or processing in intracellular compartments, viral nucleic acid or protein degradation, nuclear transport of virus or viral genome, effective to enhance rAAV transduction, with the proviso that the agent is not an inhibitor of proteosome proteolytic activity, which methods further comprise contacting the cell with an agent that alters single strand to double strand rAAV genome conversion, or ii) a method which includes contacting a mammalian cell with at least one rAAV and at least two agents in an amount effective to additively enhance rAAV transduction or a method which includes contacting the mammalian cell with at least one rAAV and at least one agent that alters rAAV endocytosis, rAAV trafficking or processing in intracellular compartments, viral nucleic acid or protein degradation, nuclear transport of virus or viral genome, effective to enhance rAAV transduction, with the proviso that the agent is not an inhibitor of proteosome proteolytic activity, which methods further comprise contacting the cell with an agent that alters cellular uptake of rAAV, Applicant provisionally elects, with traverse, specie ii.

In response to the election of species from an agent that iii) modulates microfilaments or microtubules, iv) alters cellular uptake of rAAV, v) modulates rAAV trafficking in the cell, vi) modulates rAAV processing in the cell, vii) modulates rAAV nucleic acid degradation in the cell, viii) modulates rAAV protein degradation in the cell, ix) modulates rAAV transport to the nucleus, x) modulates viral genome transport to the nucleus, xi) is not an inhibitor of proteosome proteolytic activity, or xii) modulates subcellular localization of proteosomes, Applicant provisionally elects, with traverse, specie vi.

In response to the election of species from a first agent and a second agent from xiii) an antibiotic, xiv) a chemotherapeutic, xv) a lipid-lowering compound, or xvi) a food additive, Applicant provisionally elects, with traverse, specie xiii and specie xiv.

In response to the election of two species from an agent that is epoxomicin, doxorubicin, doxil, daunorubicin, idarubicin, epirubicin, aclarubicin camptothecin, simvastatin, tannic acid, cisplatin, LLnL or Z-LLL, Applicant provisionally elects, with traverse, species doxil and LLnL.

In response to the election of species from a mammalian lung cell, a mammalian epithelial cell, a mammalian liver cell, a mammalian muscle cell, a mammalian hematopoietic cell, a mammalian heart cell, or a mammalian neuronal cell, Applicant provisionally elects, with traverse, a mammalian lung cell.

In response to the election of species from an AAV that encodes cystic fibrosis transmembrane conductance regulator (CFTR), β-globin, γ-globin, tyrosine hydroxylase, glucocerebrosidase, aryl sulfatase A, factor VIII, dystrophin or erythropoietin, Applicant provisionally elects, with traverse, CFTR.

In response to the election of species from a polypeptide encoded by a second rAAV, Applicant provisionally elects, with traverse, CFTR, where CFTR sequences are found in both AAVs.

Applicant believes claims 1-32 and 43-60 read on specie ii, specie vi, specie xiii, specie xiv, specie doxil, specie LLnL, specie mammalian lung cell, and specie CFTR.

Reconsideration and withdrawal of the Restriction Requirement, and election of species, in view of the remarks herein, is respectfully requested.

The Restriction Requirement is traversed on the basis that the inventions are closely related. That is, claims directed to a method to rAAV transduction of a mammalian cell, which includes contacting a mammalian cell with at least one rAAV and at least two agents in an amount effective to additively enhance rAAV transduction and a method to enhance rAAV transduction of a mammalian cell, which includes contacting the mammalian cell with at least one rAAV and at least one agent that alters rAAV endocytosis, rAAV trafficking or processing in intracellular compartments, viral nucleic acid or protein degradation, nuclear transport of virus or viral genome, effective to enhance rAAV transduction, with the proviso that the agent is not an inhibitor of proteosome proteolytic activity (claims 1-32 and 43-60; Group IA) are clearly related to claims directed to a method to enhance rAAV transduction of a mammalian cell, which include contacting a mammalian cell with at least one rAAV and at least two agents in an amount effective to synergistically enhance rAAV transduction and a method to enhance rAAV transduction of a mammalian cell, which includes contacting the mammalian cell with at least one rAAV and at least one agent that alters rAAV endocytosis, rAAV trafficking or processing in intracellular compartments, viral nucleic acid or protein degradation, nuclear transport of virus or viral genome, effective to enhance rAAV transduction, with the proviso that the agent is not an inhibitor of proteosome proteolytic activity (claims 1-32 and 43-60; Group IB).

The Restriction Requirement is also traversed on the basis that Restriction Requirements are optional in all cases. M.P.E.P. § 803. If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. § 803. Moreover, it is submitted that Applicant should not be required to incur the additional costs associated with the filing of multiple divisional applications in order to obtain protection for the claimed subject matter. Due to the relatedness of the subject matter of the claims in Groups IA and IB, the claims in Groups IA-IB can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner. Evidence that the claims in at least Groups IA-IB can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner is provided in the Restriction Requirement as those claims are in the same class (class 424) and subclass (subclass 932) for search purposes.

Further, as claims 1 and 43 link the inventions of Group IA and Group IB, the claims in Groups IA-IB should be examined in the same application. M.P.E.P. 809.03.

Thus, the Restriction Requirement is properly traversed. Accordingly, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

It is Applicant's position that many of the species elections do not take into consideration the claimed invention, i.e., the use of certain agents to enhance AAV transduction, and so are improper. For instance, with regard to the election of species i or ii, the invention is the use of two agents (claim 1) or an agent with particular properties (claims 33 and 43) to enhance AAV transduction in mammalian cells, optionally in conjunction with other agents, which use is not limited to a cell type to be transduced or a gene to be delivered by the AAV. It is not apparent to Applicant's Representative how an election of specie i and ii, a cell type (see, e.g., claim 16) or a polypeptide encoded by one or more rAAVs (see, e.g., claims 10 and 20), assists the Examiner in searching the claimed invention.

Nevertheless, the Examiner is requested to consider that the disclosed relationship of species i and ii is that they are agents that may be employed in methods which employ two agents or which employ agents with particular properties, to further alter AAV transduction. The disclosed relationship of species iii) - xii), species antibiotic, chemotherapeutic, a lipid-lowering compound, and a food additive, and species epoxomicin, doxorubicin, doxil, daunorubicin, idarubidin, epirubicin, aclarubicin camptothecin, simvastatin, tannic acid, cisplatin, LLnL and Z-LLL, is that these agents may be employed to enhance AAV transduction.

The disclosed relationship of the cell types is that they are all mammalian cell types, and the disclosed relationship of the polypeptide encoded by the one or more rAAVs is that they are useful in gene therapy.

Accordingly, the species elections are properly traversed, and withdrawal of all the species elections is respectfully requested.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 19th day of March 2007.

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